

inhibitors of the secondary degeneration of the nervous tissues.

The inventors of the present invention have found for the first time that ginsenoside Rb₁ or its metabolites can promote vascular regeneration and/or reconstruction, especially facilitate cerebrovascular regeneration and/or reconstruction after cerebral apoplexy, or inhibit apoptosis or apoptosis-like cell death of oligodendrocytes. Consequently, the present invention raises the possibility that ginsenoside Rb₁ or its metabolites can be used as the leading compound(s) to explore other novel active compounds or to components for prevention, treatment or therapy of diseases caused by injuries to the nervous tissues or to the spinal cord. Further, any administration routes can be selected after making prodrugs by modifying a part(s) of the chemical structure of ginsenoside Rb₁. In addition, by the identification of target molecules of ginsenoside Rb₁ or its metabolites, novel compounds, which can modify functions of the target molecules, would be synthesized, leading to the development of drugs for treatment of spinal cord injuries, neurotrauma or traumatic injuries.

Consequently, the present invention provides ginsenoside Rb₁ or its metabolites as the leading compound(s) for exploring novel active compounds or components for prevention, treatment or therapy of the diseases described hereinbefore.

Ginsenoside Rb₁ of the present invention is a compound

represented by the chemical structure depicted hereinbefore, and ginsenoside Rb_1 can be isolated and purified according to the method of Shibata et al. (Shibata S. et al., Economic and Medicinal Plant Research, World Scientific, Philadelphia, pp. 217-284, 1985). Ginsenoside Rb_1 purified by such a method has a purity more than 98%, which has been confirmed by thin-layered chromatography and nuclear magnetic resonance spectrum (Kawashima Y. and Samukawa K., J. Med. Pharmacol. Soc. Wakan-Yaku, 3, 235-236, 1986).

Ginsenoside Rb_1 of the present invention can be used in its free form, but can be used as its suitable salts. Its solvates such as hydrates can also be used.

The concentrations of ginsenoside Rb_1 used in the present invention are preferably low, as described in JP98/365560 and PCT/JP99/02550 (Brain cell or nerve cell-protective agents comprising ginsenoside Rb_1), more concretely, its concentration in extracellular fluid in lesion is 1 ng/ml or less, preferably 1 pg/ml or less, or more preferably 100 fg/ml or less. The preparations for intravenous administration of ginsenoside Rb_1 of the present invention should preferably be adjusted so that the concentrations of ginsenoside Rb_1 in the extracellular fluid of the lesion tissue of patients are maintained in the concentration range hereinabove described. Sufficient favorable effects of the pharmaceutical compositions and preparations of the present invention can be obtained even at

the concentration of 1 - 100 fg/ml in the extracellular fluid of the lesion tissue.

It was already found that intravenously administered ginsenoside Rb_1 , unlike peripherally (intraperitoneally) administered ginsenoside Rb_1 , was transferred rapidly to the central nervous system (JP98/365560 and PCT/JP99/02550: Brain cell or nerve cell-protective agents comprising ginsenoside Rb_1). The preparations for intravenous administration of the present invention may optionally be the preparations, which can be directly administered intravascularly, preferably intravenously. The preparations can be used for single intravenous infusion or continuous intravenous infusion after dissolving the present pharmaceutical compositions with physiological saline, distilled water, phosphate buffer, glucose solution, liposome or lipid microsphere. The preparations can also be a formulation, which can be used by adding to preparations for intravenous administration such as a composition for drip infusion. Further, a part(s) of the chemical structure of ginsenoside Rb_1 is modified to prepare prodrugs and a suitable route of administration or a suitable method for administration can be selected. For example, a hydroxyl group(s) in ginsenoside Rb_1 is esterified to prepare the prodrug(s), and the resulting prodrug(s) is likely to pass through the blood brain barrier, subsequently is hydrolyzed by endogenous esterase, thereby to increase the amount of